

Appl. No. : 09/748,706
Filed: : December 22, 2000

REMARKS

Claims 40, 41, 43, 45, 55-63 are presented for examination. Claims 1-39, 42, 44, and 46-54 are cancelled, Claims 40, 41, 43, and 45 are amended, and Claims 55-63 are new. Support for the amended claims and new claims can be found throughout the specification such as on page 19, lines 1-12, page 20, lines 10-11, and page 21, lines 20-34, for example. Accordingly, no new matter has been added.

Personal Interview

Applicants would like to thank the Examiner for the courteous personal interview that was conducted between Applicants' representative and the Examiner on December 2004. While no substantive agreement was reached, the Applicants and Examiner discussed the scope of the cited art in light of Applicants' claims. More specifically, Applicants' representative described the differences and advantages of Applicants' claimed method of decoding arrays technology over the cited art.

Discussion of Objection Under 37 C.F.R. §1.75(c)

The Examiner objected to Claim 49 as being of improper dependent form under 37 C.F.R. §1.75(c) for allegedly failing to further limit the subject matter of previous independent claims. The Examiner's objection is rendered moot as Claim 49 has been cancelled.

Discussion of Rejection Under 35 U.S.C. §112

The Examiner rejected Claims 40-49 under 35 U.S.C. §112, first paragraph, for allegedly failing to comply with the written description requirement. More specifically, the Examiner asserted that the term "directly attached" is not adequately supported in the specification. Applicants respectfully disagree and argue that one of ordinary skill in the art would understand from the specification that Applicants were in possession of having a ligand "directly attached" to a microsphere.

However, solely to advance prosecution, Applicants have amended Claim 40 to recite that the IBLs are "attached" to the microsphere. This term is used throughout the specification such that those skilled in the art would understand that Applicants were in possession of attaching

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IBLs to the microsphere. For the above reasons, Applicants respectfully request the withdrawal of this rejection.

Discussion of Rejection Under 35 U.S.C. § 102

The Examiner rejected Claims 40-45 and 47-53 under 35 U.S.C. § 102(b) as allegedly being anticipated by WO 97/14028 (Chandler). Applicants respectfully traverse because Chandler does not disclose each and every element of the claimed invention.

To be anticipatory under 35 U.S.C. § 102, a reference must teach each and every element of the claimed invention. *See Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1379 (Fed. Cir. 1986). "Invalidity for anticipation requires that all of the elements and limitations of the claim are found within a single prior art reference. ...There must be no difference between the claimed invention and the reference disclosure, as viewed by a person of ordinary skill in the field of the invention." *See Scripps Clinic & Research Foundation v. Genentech, Inc.*, 927 F.2d 1565 (Fed. Cir. 1991).

Applicants' claims relate to methods of decoding the positions of bioactive agents that are attached to microspheres of a bead array. As many bead arrays are made by randomly distributing beads onto the array, it is sometimes necessary to determine the position of the randomly distributed beads in order to determine where a particular bead, and its attached bioactive agent, are located. In the claimed methods, the microspheres comprise a unique combination of identifier binding ligands that have been assigned to a particular bioactive agent. By determining the combination of identifier binding ligands attached to a microsphere, one can thereby determine the bioactive agent associated with the microsphere. In one embodiment, the identifier binding ligands on the microsphere are identified by contacting the array with one or more decoder binding ligands that are designed to specifically bind to the identifier binding ligands.

As mentioned above, Claims 42, 44, and 46-53 are cancelled, so this rejection is moot with respect to these claims. The pending claims, Claims 40, 41, 43, 45, and 55-63, are directed to methods of decoding the position of bioactive agents attached to microspheres on an array substrate. *See Application*, page 21, lines 20-33.

The Office Action mailed July 16, 2004, asserts that Chandler disclosed a method comprising providing an array composition comprising microspheres having a first and second

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IBL. *See* Office Action, page 6. However, as acknowledged in the Office Action, Chandler only discloses microspheres having multiple copies of the same IBL. Accordingly, this cited reference fails to teach or suggest using a combination of at least two different IBLs on the same microsphere, as the claimed methods recite.

As set forth in Applicants' specification, the use of a combination of multiple IBLs on each microsphere provides tremendous advantages. When only one IBL is attached to a microsphere and the number of DBLs that are used equals the number of unique IBLs then a heavy burden is placed on a practitioner to obtain a large number of different types of DBLs.

In comparison, and as further pointed out in Applicants' specification, by using more than one IBL on a microsphere to identify a bioactive agent, a practitioner does not have to obtain as many different types of IBLs and DBLs. The following example helps clarify the advantages of attaching more than one IBL per microsphere. If 1024 different microspheres each contained one of 1024 different bioactive agents, and only one IBL was being used, a practitioner would have to obtain 1024 different IBLs, attach one to each microsphere and then use 1024 different DBLs to detect each IBL.

In contrast, if the practitioner assigned 10 IBLs per bead, he could generate a 10 bit binary code, where each bit can be designated as "1" (IBL is bound to a DBL) or "0" (IBL is not bound to a DBL). A 10 bit binary code has 2^{10} possible variants. The mathematical formula is as follows: $2^n = y$ (Where "n" equals the number of different IBLs on a bead and "y" = the number of bioactive agents that can be encoded). In the above example $2^{10} = 1024$. Thus, a practitioner could encode the same amount of bioactive agents by using only 10 IBLs per bead. Additionally, the practitioner would only have to obtain 10 different DBLs to decode the array.

In particular embodiments, a series of DBLs can be bound to the array sequentially, and the binding pattern of those DBLs to the IBLs thereafter analyzed. *See* Application, page 21, lines 20-33, and pages 29-31. By analyzing which IBLs bound, and which IBLs didn't bind to particular DBLs, one can determine the identity of each microsphere, and thereby its bioactive agent.

As there is no teaching or suggestion in Chandler to using microspheres each having a plurality of different IBLs, this reference cannot anticipate Claims 40, 41, 43, 45, and 55-63. For this reason, Applicants respectfully request the withdrawal of this rejection.

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Discussion of Rejection Under 35 U.S.C. § 103

The Examiner rejected Claim 46 under 35 U.S.C. § 103(a) as allegedly being obvious over Chandler in view of U.S. Patent No. 6,060,240 (Kamb). In addition, the Examiner rejected Claim 54 under 35 U.S.C. §103(a) as being unpatentable over Chandler in view of Biomagnetic Techniques in Molecular Biology, technical handbook, 1998, page 165 (Dynal®). Applicants respectfully disagree.

To establish a *prima facie* case of obviousness a three-prong test must be met. First, there must be some suggestion or motivation, either in the references or in the knowledge generally available among those of ordinary skill in the art, to modify the reference. Second, there must be a reasonable expectation of success found in the prior art. Third, the prior art must teach or suggest all the claim limitations. *In re Vaeck*, 947 F.2d 488 (Fed. Cir. 1991).

While these rejections are moot with respect to Claims 46 and 54, as both of these claims are cancelled, Applicants respectfully submit that the cited art fails to teach or suggest each element of the pending claims. As stated above, Claims 40, 41, 43, 45, and 55-63, are directed to methods of decoding the position of bioactive agents attached to microspheres distributed on an array substrate. More specifically, the claimed methods utilize a combination of different IBLs on a microsphere that correspond to an attached bioactive agent. *See* Application, page 21, lines 20-33. In contrast to Applicants' claims, the Examiner has failed to cite any passages in Chandler, Kamb or Dynal®, that teach a microsphere having two different IBLs that correspond to a particular bioactive agent. For these reasons, Applicants respectfully request withdrawal of the rejections under 35 U.S.C. § 103, and allowance of the pending application.

CONCLUSION

Applicants have endeavored to address all of the Examiner's concerns as expressed in the outstanding Office Action. Accordingly, amendments to the claims, the reasons therefore, and arguments in support of the patentability of the pending claim set are presented above. Any claim amendments which are not specifically discussed in the above remarks are made in order to improve the clarity of claim language, to correct grammatical mistakes or ambiguities, and to otherwise improve the capacity of the claims to particularly and distinctly point out the invention to those of skill in the art. In light of the above amendments and remarks, reconsideration and withdrawal of the outstanding rejections is specifically requested.

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Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410. If the Examiner finds any remaining impediment to the prompt allowance of these claims that could be clarified with a telephone conference, the Examiner is respectfully requested to initiate the same with the undersigned.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: 1/18/05

By: Marc Baumgartner
Marc Baumgartner
Registration No. 53,976
Attorney of Record
Customer No. 20,995
(619) 235-8550

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